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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,761	02/21/2006	Takamasa Watanabe	0020-5502PUS1	6669

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EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
01/30/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/568,761	WATANABE ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19,20,31 and 32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-20 and 31-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/17/08 has been entered.

2. Claims 19, 20, 31 and 32 are pending and under examination in the instant application.

3. The Cruse and Katz references cited on the PTO FORM 892 is provided by Applicant on 11/17/08 and will not be supplied.

4. Applicant's cancellation of "which blocks a biological activity of CD81" have obviated the previous Written Description rejection under 35 U.S.C 112. Accordingly, the Examiner will not address the Watanabe declaration under Rule 1.132, filed 11/17/08.

5. In view of the amendment filed on 11/17/08, only the following rejections are remained.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 19-20 and 32 stand rejected under 35 U.S.C. 102(b) as being anticipated by U.S Pat. No. 6,423,501.

The `501 patent teaches a method of treating inflammatory condition in a mammal comprising administering to the mammal an effective amount of an agent which induces CD81-mediated signal transduction. For example, the method can be used to treat inflammatory responses associated with disorders such inflammatory bowel disease (i.e., Crohn's disease and ulcerative colitis) (see col., 13, lines 34-45 in particular). The `501 patent teaches that agents described herein can be anything which binds to or interacts with CD81 and induces (i.e., activates) or enhances CD81-mediated signal transduction. For example, the agent can be a polyclonal or monoclonal antibody, such as an anti-CD81 antibody. In particular embodiments, the antibody is 5D1 or 1A12 (see col., 9, line 65 to col., 10, line 3 in particular). The `501 patent further teaches that injections of anti-CD81 yielded significant inhibition of PCA reactions (blocks a biological activity of CD81) (see FIG. 10B). The functional properties claimed in claim 32 are inherent.

The reference teachings anticipate the claimed invention.

8. Claims 19-20 and 32 stand rejected under 35 U.S.C. 102(b) as being anticipated by WO 98/25647 (IDS ref. No. BJ).

The `647 publication teaches a method of treating inflammatory condition in a mammal comprising administering to the mammal an effective amount of an agent which induces CD81-mediated signal transduction. For example, the method can be used to treat inflammatory responses associated with disorders such inflammatory bowel disease (i.e., Crohn's disease and ulcerative colitis) (see col., 26, lines 12-22 in particular). The `501 patent teaches that agents described herein can be anything which binds to or interacts with CD81 and induces (i.e., activates) or enhances CD81-mediated signal transduction. For example, the agent can be a polyclonal or monoclonal antibody, such as an anti-CD81 antibody. In particular embodiments, the antibody is 5D1 or 1A12 (see Pg. 19, line 3-9 in particular). The `647 publication further teaches that injections of anti-CD81 yielded significant inhibition of PCA reactions (blocks a biological activity of CD81) (see FIG. 10B). The functional properties claimed in claim 32 are inherent.

The reference teachings anticipate the claimed invention.

Applicant's arguments, filed 11/17/08, have been fully considered, but have not been found convincing.

Although the Examiner alleged that the prior art reference discloses a method for treating an inflammatory condition in a mammal comprising administering to the mammal an effective amount of an agent which blocks a biological activity of CD81, '501 fails to effectively show that an anti-CD81 antibody can be used for the treatment or improvement of IBD. Please note that the amended claim 19 does not have the expression "which blocks a biological activity of CD81 ." Therefore, what claim 19 recites is the administration of the anti-CD81 antibody for the treatment of IBD per se.

However, a reference contains an "enabling disclosure" if the public was in possession of the claimed invention before the date of invention. "such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his own knowledge to make the claimed in invention." In re Donohue, 766 F.2d 531,226 USPQ 619 (Fed. Cir. 1985). See MPEP 2121.01. Further, if the prior art teaches the identical chemical structure (i.e., anti-CD81 antibody), the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Applicants submit that though '501 lists using the antibodies of Fleming to treat IBD, IBD is one of over 20 possible conditions found in that single paragraph. Thus, one of skill is given no direction as to whether the antibodies inhibiting CD-81 cell mediated signal transduction are intended to increase or decrease any mechanisms or effects of IBD, or if they would work at all.

However, it is noted that in order to constitute anticipatory prior art, a reference must identically disclose the claimed method. The prior art of the `501 patent and the `647 publication teach a method of treating IBD with anti-CD81 antibodies.

Moreover, the experimental results of'501 are not meaningful in light of a treatment of IBD. '501 discloses that anti-CD81 antibody 5D1 and 1A12 inhibited in vitro mast cell degranulation using the RBL-2H3 cell line ('501 col. 19, lines 27-30), as well as in vivo IgE mediated mast cell degranulation using the passive cutaneous anaphalixis (PCA) reaction in rat. ('501, col. 11, line 54 to col. 12, line 11). Those results support that anti-CD81 antibody can inhibit FcγRI-induced mast cell degranulation and therefore, is useful for the treatment of an allergy. Although '501 dislcoses that an agent which induces CD81 mediated signal transduction is useful for the treatment of inflammatory responses associated with disorders associated with disorders such as IBD, '501 fails to show the effect of the agent which induces CD81 mediated signal transduction or the effect of an anti-CD81 antibody on conditions associated with IBD.

However, the standard for what constitutes sufficient enablement of prior art reference for purpose of anticipation under 35 U.S.C. 102(b) differs from enablement standard under Section 112, in that the prior art reference need not demonstrate utility in order to serve as anticipating reference under Section 102. Here, `501 patent and the `647 publication are enabling in the sense that they describes the claimed invention sufficiently to enable a person of ordinary skill in the art to carry out the claimed method of treating IBD in mammal with an anti-CD81 antibody. Essentially, applicants are applying a higher standard of enablement to the anticipatory reference than is warranted.

PCA is a well known procedure to screen agents for the treatment of type I hypersensitivity or alltergy. (See attached, Cruse, Atlas of Immunology, 1999, pages 225-234). On page 233, col. 2, line 15 from the bottom of the page to page 234, col. 1, line 2, the passive cutaneous anaphylaxis (PCA) is explained as an in vivo test for type I immediate hypersensitivity. There have been an enormous number of agents that were evaluated as positive in the PCA test and developed as anti-allergic agents. As far as Applicants know, none of them has been marketed as a treatment for of IBD, even to date. If an agent was positive in the PCA test or useful for the treatment of an allergy, the art would not expect that the agent is useful for the treatment of IBD.

However, the mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Even though applicant has proposed or claimed the mechanism by which an anti-CD81 antibody alleviates symptoms of IBD does not appear to distinguish the prior art teaching the same methods to achieve the same end result. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

As is discussed in the background art section of the original Specification, there was no satisfactory pharmacotherapy for IBD at the filing date. The situation has not been changed yet. The J. Clin. Gastroenterol., is a review of the drugs for the treatment of IBD. (See attached, Katz, J. Clin. Gastroenterol. Vol. 41, 2007, pages 799-809). Many drugs are discussed in this article, but no anti-allergy drugs are listed. No satisfactory treatment for IBD has yet been developed even as of late 2007.

However, evidence of secondary considerations, such as advantages not appreciated by the prior art, unexpected results, solution of a long-felt need, and the like, is irrelevant to 35 U.S.C. 102 rejections and thus cannot overcome a rejection so based. See MPEP 2131.04.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

10. Claim 31 is rejected under 35 U.S.C. 103(a) as being unpatentable over U.S Pat. No. 6,423,501 or WO 98/25647 as applied to claims 19-20 and 32 bove and further in view of and Owens *et al* (1994).

The teachings of Pat. No. 6,423,501 or WO 98/25647 publication have been discussed, supra.

The claimed invention differs from the reference teachings only by the recitation of and Fab, F(ab`)2 or Fv or scFv in claim 31.

Owens *et al* teach the modification of murine antibodies such as a single chain antibody, a Fab fragment, a $F(ab')_2$ fragment. Owens *et al* further teach that antibody fragments are the reagents of choice for some clinical applications, and the chimeric antibodies offers the ability to mediate antigen-dependent cytotoxicity and complement –dependent cytotoxcity (see the entire document).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the anti–CD81 antibody taught by 6,423,501 or WO 98/25647 to Fab or F(ab')2 fragments taught by Owens et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the antibody fragments are the reagents of choice for some clinical applications and the chimaeric antibodies offers the ability to mediate antigen-dependent cytotoxicity and complement-dependent cytotoxcity as taught by Owens *et al*.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art

would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments, filed 11/17/08, have been fully considered, but have not been found convincing.

Applicant submits that '501 only teaches those skilled in the art how to treat allergic reactions and does not at all suggest how any agents described therein would affect IBD. Owens does not teach anything about treating IBD, so no combination of the references would teach the use of an anti-CD81 antibody for the treatment of IBD.

The Examiner's position is that the `501 and `647 teach those skilled in the art how to treat IBD with anti-CD81 antibodies, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the anti-CD81 antibodies taught by the `501 or `647 to generate the claimed antibody fragments.

11. New Ground of rejections.

12. Claims 19-20 and 31-32 stand rejected under 35 U.S.C. 102(b) as being anticipated by Curd et al (WO 00/67796).

Curd et al teach treatment of inflammatory bowel disease, Crohn's disease and ulcerative colitis with anti-CD81 antibody (see published claims 1, 2, 3, 6). The various functional activities recited in the claims are inherently found in said method the method taught by Curd et al teaches in vivo administration of the same antibody recited in the claims to treat the same disease recited in the claims. Curd et al teach the claimed antibody fragments (see page 4, lines 38-40).

The reference teachings anticipate the claimed invention.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen B. O'Hara can be reached on (571) 272-0878. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

January 26, 2009

/Maher M. Haddad/
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